REMARKS

Claims 19-26 were rejected and remain pending. In light of the following remarks, Applicants respectfully request reconsideration and allowance of claims 19-26.

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 19-26 under 35 U.S.C. § 112, first paragraph, allegedly because "the specification, while being enabling for a method comprising a) transfecting a cell with a nucleic acid sequence encoding a protein operably linked to a tetracycline regulatable promoter *in vitro*, and b) increasing expression of the protein using tetracycline *in vitro*, does not reasonably provide enablement for administering the cells to a mammal that has had an immune response against the protein." This conclusion is apparently based on the Examiner's interpretation that the present claims require obtaining a therapeutic effect via successful gene therapy.

Applicants respectfully disagree. Claim 19 recites a method of regulating the expression of a nucleic acid sequence encoding a polypeptide which is immunogenic in a mammal, wherein the mammal has already made an immune response to the polypeptide. This method includes (a) obtaining a cell comprising a vector comprising a drug-regulatable promoter operably linked to the nucleic acid sequence encoding the polypeptide, (b) introducing the cell into the mammal, and (c) increasing expression of the polypeptide as a result of altering the amount of regulatory drug to which the cell is exposed. At no point does this claim require achieving the status of a gene therapy "success story." In contrast to the Examiner's assertion that the only disclosed purpose for the recited methods is for therapy, Applicants note that a person having ordinary skill in the art reading Applicants' specification would have appreciated that one purpose for the presently claimed method is to provide a way for cells designed to express an immunogenic polypeptide to avoid a mammal's pre-existing immune response to that immunogenic polypeptide. It would have been apparent to the skilled artisan that such methods would have been useful for many reasons other than obtaining a successful gene therapy outcome. For example, the *in vivo* effects of any polypeptide, whether therapeutic or non-therapeutic, that

happens to be immunogenic to a mammal can be assessed using the methods provided in Applicants' specification.

Applicants also note that the relevance of the cited references regarding gene therapy is questionable. For example, the Crystal reference was apparently cited for the notion that to enable the presently claimed invention, one must design the ideal vector by overcoming hurdles such as "the need to increase the efficiency of gene transfer, to increase target specificity and to enable the transferred gene to be regulated." Applicants note that the presently claimed invention recites (a) obtaining a cell comprising a vector comprising a drug-regulatable promoter operably linked to the nucleic acid sequence encoding the polypeptide and (b) introducing that obtained cell into the mammal. Thus, there is no need for high efficiency *in vivo* gene transfer of a vector and no need for increased *in vivo* target specificity of the vector. The recited cells can be obtained by performing standard *in vitro* nucleic acid transfer techniques such as those disclosed in Applicants' specification. *See*, the section extending from page 7, line 32 to page 8, line 6 as well as page 24, lines 27-29. In addition, Applicants' specification discloses multiple drug-regulatable promoters that can be operably linked to nucleic acid sequence encoding a polypeptide. *See, e.g.*, page 10, lines 9-12. Moreover, Example 1 demonstrates that the expression of the polypeptide can be regulated by altering the amount of regulatory drug to which the cells are exposed.

Further, a person having ordinary skill in the art reading Applicants' specification would have been able to make and use the presently claimed invention without undue experimentation. For example, no undue experimentation is required for a person having ordinary skill in the art to obtain a cell having a vector containing a drug-regulatable promoter operably linked to nucleic acid encoding a polypeptide. This is particularly true given that Applicants' specification discloses multiple drug-regulatable promoters that can be operably linked to nucleic acid encoding a polypeptide. *See, e.g.*, page 10, lines 9-12. In addition, no undue experimentation is required for a person having ordinary skill in the art to introduce those obtained cells into a mammal. In fact, a person having ordinary skill in the art could have easily infused or injected the cells into a mammal's blood stream as disclosed on page 20, lines 9-12 of Applicants'

specification. Moreover, no undue experimentation is required for a person having ordinary skill in the art to increase expression of the polypeptide by altering the amount of regulatory drug to which the cells are exposed. This is particularly true given that many drug regulatable promoters were well known and characterized in the art. For example, the tetracycline-regulatable promoter is a promoter that was routinely used to regulate polypeptide expression in response to tetracycline. In addition, Applicants' specification discloses using a tetracycline-regulatable promoter to regulate polypeptide expression by altering the amount of tetracycline to which the cells are exposed. See, e.g., Example 1. Thus, taken together, Applicants' specification fully enables the presently claimed invention.

In light of the above, Applicant respectfully requests the withdrawal of the rejection of claims 19-26 under 35 U.S.C. § 112, first paragraph.

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 19-26 under 35 U.S.C. § 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter applicant regards as the invention. Specifically, the Examiner stated that (1) what the Applicants mean by "altering the amount of regulatory drug" in step (c) cannot be determined and (2) the specification does not define what the term "altering" means.

Applicants respectfully disagree. A person having ordinary skill in the art reading Applicants' specification would have understood the meaning of the term "altering" and the phrase "altering the amount of regulatory drug." This is particularly true given that page 6, line 20 of Applicants' specification discloses that "[a]ltering the concentration means increasing or decreasing the amount."

In light of the above, Applicants respectfully request the withdrawal of the rejection of claims 19-26 under 35 U.S.C. § 112, second paragraph.

CONCLUSION

Applicant submits that claims 19-26 are in condition for allowance, which action is requested. The Examiner is invited to call the undersigned attorney at the telephone number below if such will advance prosecution of this application. The Commissioner is authorized to charge any fees or credit any overpayments to Deposit Account No. 06-1050.

Respectfully submitted,

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